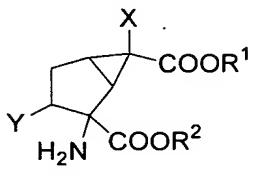
CLAIM

We claim:

1. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [I]



[I]

[wherein R^1 and R^2 are the same or different, and each represents a hydrogen atom, a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a C_{1-10}alkyl group substituted by one or two phenyl groups, a C_{2-10}alkenyl group, a C_{2-10}alkynyl group, a hydroxylC_{2-10}alkyl group, a C_{1-10}alkoxycarbonylC_{1-10}alkyl group, an aminoC_{2-10}alkyl group or a C_{1-10}alkoxyC_{1-10}alkyl group;

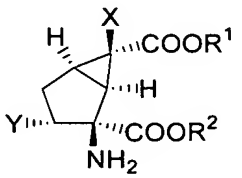
X represents a hydrogen atom or a fluorine atom;

Y represents an amino group, $-SR^3$, $-S(O)_nR^7$, $-SCHR^3R^4$, $-S(O)_nCHR^3R^4$, $-NHCHR^3R^4$, $-N(CHR^3R^4)(CHR^5R^6)$, $-NHCOR^3$ or $-OCOR^7$ (wherein R^3, R^4, R^5 and R^6 are the same or different, and each represents a hydrogen atom, a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents "a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C_{1-10}alkyl group, a C_{1-10}alkoxy group and a trifluoromethyl group";

R^7 represents a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents "a phenyl group substituted by one to five substituents selected from a group consisting of a

halogen atom, a phenyl group, a C_{1-10}alkyl group, a C_{1-10}alkoxy group and a trifluoromethyl group"; and n represents integer 1 or 2)].

2. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II]



[Ⅱ]

[Wherein R^1 and R^2 are the same or different, and each represents a hydrogen atom, a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a C_{1-10}alkyl group substituted by one or two phenyl groups, a C_{2-10}alkenyl group, a C_{2-10}alkynyl group, a hydroxylC_{2-10}alkyl group, a C_{1-10}alkoxycarbonylC_{1-10}alkyl group, an aminoC_{2-10}alkyl group or a C_{1-10}alkoxyC_{1-10}alkyl group;

X represents a hydrogen atom or a fluorine atom;

Y represents an amino group, $-SR^3$, $-S(O)_nR^7$, $-SCHR^3R^4$, $-S(O)_nCHR^3R^4$, $-NHCHR^3R^4$, $-N(CHR^3R^4)(CHR^5R^6)$, $-NHCOR^3$ or $-OCOR^7$ (wherein R^3, R^4, R^5 and R^6 are the same or different, and each represents a hydrogen atom, a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents "a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C_{1-10}alkyl group, a C_{1-10}alkoxy group and a trifluoromethyl group";

R^7 represents a C_{1-10}alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group or represents "a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C_{1-10}alkyl group, a C_{1-10}alkoxy group and a trifluoromethyl group"; and n represents integer 1 or 2)].

3. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^2 represents a hydrogen atom.

4. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom.

5. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom; and
X represents a fluorine atom.

6. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom; and
X represents a hydrogen atom.

7. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents $-SR^3$ ($-SR^3$ is the same as mentioned above).

8. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and

Y represents -$S(O)_nR^7$ (-$S(O)_nR^7$ is the same as mentioned above).

9. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents –$SCHR^3R^4$ (-$SCHR^3R^4$ is the same as mentioned above).

10. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents -$S(O)_nCHR^3R^4$ (-$S(O)_nCHR^3R^4$ is the same as described above).

11. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents –$NHCHR^3R^4$ (-$NHCHR^3R^4$ is the same as mentioned above).

12. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents -$N(CHR^3R^4)(CHR^5R^6)$ (-$N(CHR^3R^4)(CHR^5R^6)$ is the same as mentioned above).

13. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula

[II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-NHCOR^3$ ($-NHCOR^3$ is the same as mentioned above).

14. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-OCOR^7$ ($-OCOR^7$ is the same as mentioned above).

15. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-SR^3$ ($-SR^3$ is the same as mentioned above).

16. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-S(O)_nR^7$ ($-S(O)_nR^7$ is the same as mentioned above).

17. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 andR^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-SCHR^3R^4$ ($-SCHR^3R^4$ is the same as mentioned above).

18. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim

2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-S(O)_nCHR^3R^4$ ($-S(O)_nCHR^3R^4$ is the same as mentioned above).

19. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-NHCHR^3R^4$ ($-NHCHR^3R^4$ is the same as mentioned above).

20. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-N(CHR^3R^4)(CHR^5R^6)$ ($-N(CHR^3R^4)(CHR^5R^6)$ is the same as mentioned above).

21. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-NHCOR^3$ ($-NHCOR^3$ is the same as mentioned above).

22. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-t-butylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclo

[3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid; or

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid.

23. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

(1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-t-butylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicycl

o [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 6-isobutyl ester; or

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 6-benzyl ester.

24. A drug comprising the 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to any one of claims 1 to 23, the pharmaceutically acceptable salt thereof or the hydrate thereof as an active ingredient.

25. The drug according to claim 24 wherein the drug is a Group II metabotropic glutamate receptor antagonist.